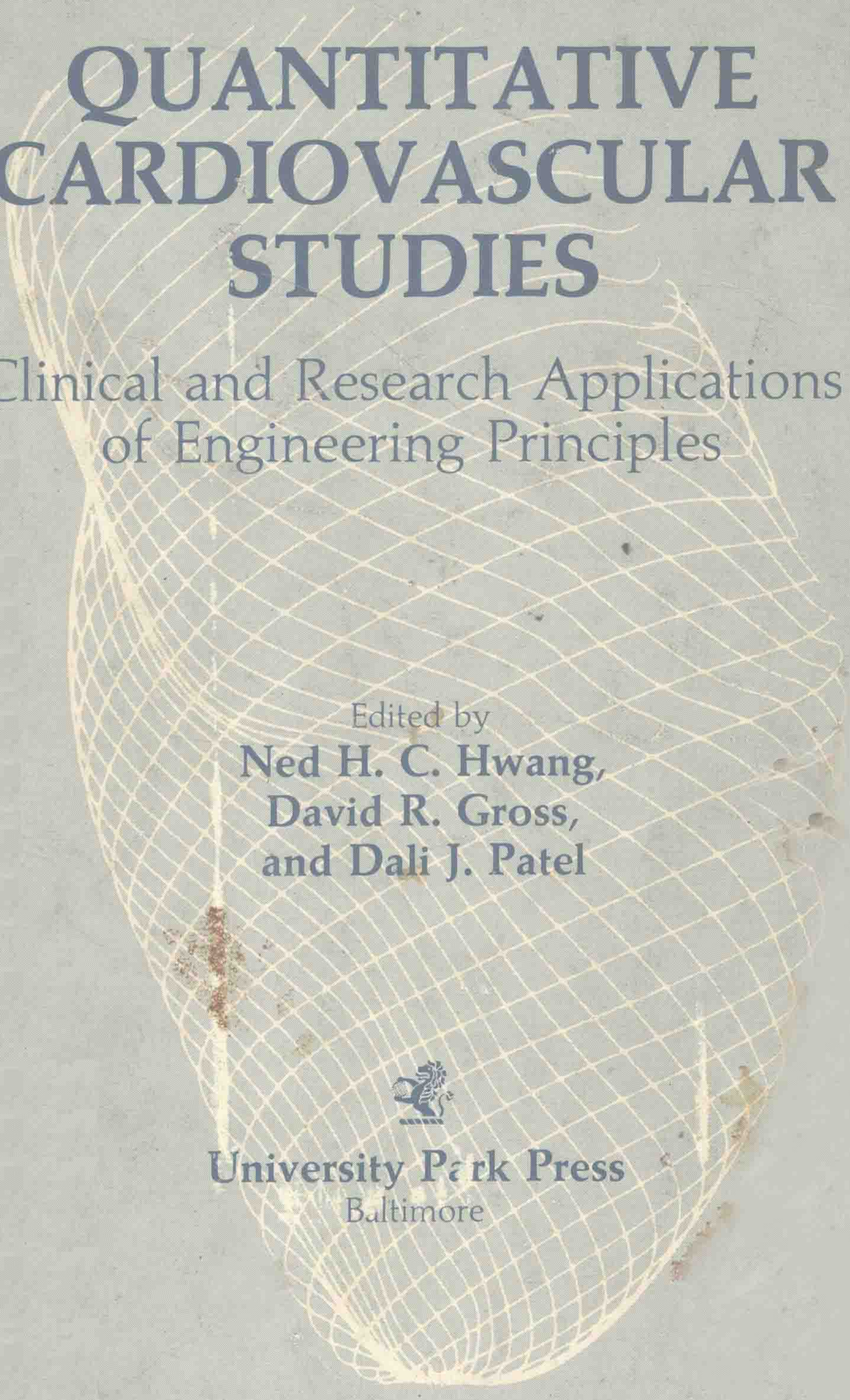

QUANTITATIVE CARDIOVASCULAR STUDIES

Clinical and Research Applications of Engineering Principles

Edited by

Ned H. C. Hwang, David R. Gross, and Dali J. Patel

University Park Press
Baltimore

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UNIVERSITY PARK PRESS
International Publishers in Science, Medicine, and Education
233 East Redwood Street
Baltimore, Maryland 21202

Typeset by American Graphic Arts Corporation.
Manufactured in the United States of America by The Maple Press Company.

Library of Congress Cataloging in Publication Data
Main entry under title:

Quantitative cardiovascular studies.

Includes index.
1. Cardiovascular system—Mathemetical models.
2. Heart—Mathematical models. 3. Hemodynamics—Mathematical models. 4. Biomedical engineering.
I. Hwang, Ned H. C. II. Gross, David R.
III. Patel, Dali J. [DNLM: 1. Cardiovascular system—Congresses. 2. Biomedical engineering—Congresses. 3. Research—Congresses. WG110 Q1 1975]
QP102.Q36 612.'1 78-25768
ISBN 0-8391-1273-4

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Dedication

The scientific affairs division of the North Atlantic Treaty Organization annually sponsors advanced study institutes covering a wide range of scientific topics. In 1975, the first NATO advanced study institute on cardiovascular research was organized by Ned H. C. Hwang and was held at the University of Houston, Houston, Texas. As a result of that meeting, a textbook entitled *Cardiovascular Flow Dynamics and Measurements* was edited by N. H. C. Hwang and N. A. Normann, and was published by University Park Press.

The present text is a result of the second of this series of institutes, held in Urbino, Italy, for two weeks during September/October of 1977. This latest advanced study institute was entitled "Engineering Principles in Cardiovascular Research."

The general format of these institutes is tutorial. Lecturers are selected on the basis of their recognized expertise in the subject of their presentation. Participants are selected on a competitive basis from primarily NATO membership countries. Young investigators with proven credentials in relevant areas of cardiovascular research were chosen from both life and physical sciences to attend the 1977 NATO Institute.

Each lecturer was provided with 1½ or 3 hours for his presentation. With this amount of time, an in-depth review of the basic and recent developments in each field was possible. In addition, several evening panel discussions were held in which lecturers further demonstrated the interrelationships of the various specialities.

We feel priveleged to edit this text. We would like to thank the NATO Scientific Affairs Division for their continued support of this concept. We dedicate this text to their most worthwhile effort.

Preface

This book contains four parts: Part I presents engineering principles applied to basic cardiovascular physiology; Part II presents engineering principles in blood rheology, thromboembolism and microcirculation; Part III presents specific topics in cardiovascular flow dynamics; and Part IV discusses some practical applications of engineering principles in cardiology.

The first chapter in Part I of this text serves both as an introduction to the book and as a discussion of animal models. In this chapter certain statements concerning animal models are in conflict with concepts expressed in subsequent chapters; in our opinion, this serves to emphasize that many details of cardiovascular modeling have yet to be adequately quantified. In Chapter 2 Kenner lucidly discusses various physical and mathematical models of the cardiovascular system. His own original work is responsible for many of the important developments in this field, and therefore uniquely qualifies Professor Kenner for this task. In Chapter 3 Westerhof, Murgo, and their colleagues review the concept of arterial impedance and its clinical application. Their data include pressure-flow measurements from the ascending aorta of man. From these they compute input impedance during rest, exercise, and various physiological maneuvers. In Chapter 4 Bergel and Hunter review the field of cardiac muscle mechanics. They present a new mathematical approach to analyzing such problems. The theory takes into account previously known relationships and uses these to predict the behavior of the intact heart. In Chapter 5 Patel, Vaishnav, and Atabek discuss the role of mechanical factors in atherogenesis. They first present methods for studying discrete local properties of the intimal layer of an artery, and then describe a nonlinear method for computing local flow fields in vivo.

The second part of the book, Chapters 6 through 9, is devoted to a review of the microrheology of blood and its applications. In Chapter 6 Chien reviews the basic physical concepts of blood rheology, including blood viscosity, deformability of red blood cells and red cell aggregation. In Chapter 7 Goldsmith and Karino discuss the role of fluid mechanical factors in both thrombosis and atherosclerosis from a macroscopic as well as a microrheological point of view. In Chapter 8 Schmid-Schönbein and co-workers discuss the application of basic microcirculatory and hemorheological concepts to clinical and physiological problems. In Chapter 9 Martin and his colleagues discuss the effects of shear stress and mechanical trauma on the morphology and function of human polymorphonuclear leukocytes.

Part III of the book, Chapters 10 through 12, is devoted to specific topics in cardiovascular flow dynamics. In Chapter 10 Oddou and his colleagues discuss certain nonlinear aspects of wave propagation in arterial systems, using some of their experimental data. In Chapter 11 Hwang and van Hoften provide a systematic review of current techniques available for measurement and analysis of blood turbulence. Specifically, they discuss the use of the laser anemometer, the hot-film anemometer, and the multiple-gated ultrasonic Doppler velocimeter. In Chapter 12 Reul and Talukder discuss their point of view concerning heart valve mechanics. These concepts, although somewhat unconventional, might prove useful in the design of the next generation of valvular prostheses.

Part IV, Chapters 13 through 18, presents some practical applications of engineering principles. In Chapter 13 Greatbatch provides an interesting review of cardiac pacemakers. He discusses the advantages of the battery-powered pacemaker over the nuclear-powered pacemaker, and presents a rigorous cumulative analysis and a random linear failure analysis in detail. In our opinion, these statistical methods could be readily adapted for clinical studies. In Chapter 14 Monti presents the current status of oxygenator research in his laboratory. He also discusses general characteristics of various types of extracorporeal oxygenators. In Chapter 15 Färber discusses the use of microprocessors in clinical cardiology. We see many future applications in cardiovascular research for this technology. In Chapter 16 Brower and Meester describe the use of their computerized catheterization laboratory with its automatic data processing capabilities. In Chapter 17 Kalmanson and Veyrat describe the use of echo-Doppler velocimetry in clinical cardiology. Their pioneering work in measuring intracardiac turbulence as a diagnostic tool is noteworthy. In Chapter 18 Akutsu and Jarvik discuss their respective artificial heart programs. Finally, Blackshear captures the flavor and spirit of the NATO Institute that generated this text.

In summary, this book provides an in-depth review of recent advances in quantitative cardiovascular research. We hope that the material included will be useful to both clinicians and research scientists. It could also be easily adapted as a textbook for a one-semester graduate course.

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Part I

Chapter 1

Animal Models in Cardiovascular Research

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COMPARATIVE CHARACTERISTICS OF THE CARDIAC PUMP AND VASCULAR DISTRIBUTION SYSTEM
- **Gross Anatomy**
- **Histological and Biochemical Properties**
- **Activation and Conduction Processes**
- **Comparative Characteristics of the Elastic and Muscular Vessels**

SPECIAL CONSIDERATIONS ASSOCIATED WITH PARTICULAR STUDIES

SPECIFIC DISEASE MODELS
- **Congenital Defects**
- **Inheritable Predilection**
- **Spontaneous Hypertension and Atherosclerosis**

HEART FAILURE MODELS

CONCLUSIONS

A rather well-known physiologist by the name of Claude Bernard wrote in 1856: ". . . two things must be considered in the phenomenon of life: first the fundamental properties of vital units which are general; then arrangements and mechanisms in organization which give each animal species its peculiar anatomical and physiological form. . . . Certain animals. . . offer favorable anatomical arrangements or special susceptibility to certain influences."

Investigators into the secrets of the design and function of the cardiovascular system have used the concept of similarity in fundamental properties to make huge strides in our understanding of this system. As we move from the general to the specific in our investigations, it is apparent that differences in "arrangements and mechanisms in organization" may cause us to arrive at specific conclusions that do not necessarily hold for the general case. Data collected on rabbit atria, dog carotid arteries, isolated cat papillary muscles, or Starling preparation rat hearts may or may not be applicable to the human situation.

The purpose of this chapter is to point out some of the obvious differences that exist between and among various animal models currently used in cardiovascular research. The authors represented in this text are engineering-oriented cardiologists, physiologists, and engineers whose approach is problem solving. The secrets we hope to unlock and the problems we hope to solve are all related to the human condition. With this in mind it is obvious that we must be aware of those limits that define "fundamental properties" and with the signs that indicate that we are dealing with specific details of "arrangements and mechanisms in organization" that characterize the particular animal model being used.

It must be made clear that there is very little enthusiasm or support for a study of animal models per se. The interest and responsibility for this rest, quite properly, with the researcher who has a specific problem under investigation. It is each investigator's responsibility to ensure that the animal model chosen is appropriate and that the specific detailed characteristics of that particular model are carefully identified.

Unfortunately the choice of animal model often seems to be dictated by considerations that have very little to do with the problem at hand. Foremost in this decision-making process seem to be familiarity with the model, housing requirements and the availability of space, equipment, management expertise, and cost. From the scientific point of view all of these considerations, except perhaps familiarity with the model, are not justifiable. Although it is important to be familiar with the particular physiological traits and responses of a species before using it in a study, a choice of animal model dictated primarily by this criterion is not acceptable.

The proper choice of animal model requires a very careful definition of the problem to be solved. For example, if one is interested in conduction abnormalities in the human heart it is worse than naive to use an animal model with a completely different specialized conduction system.

COMPARATIVE CHARACTERISTICS OF THE CARDIAC PUMP AND VASCULAR DISTRIBUTION SYSTEM

Gross Anatomy

Obviously species differences in gross anatomy exist. These include variations in position of the heart within the thorax, as well as size, shape, and configuration variations. The differences can be important, depending upon the investigations being conducted. As discussed in Chapter 18, partial cardiac bypass devices and totally artificial hearts require a certain amount of available space within the thorax. Evaluating prosthetic conduits and valves requires an animal model that closely approximates the size and configuration of human anatomy. Cardiovascular devices must be of a size and output capability similiar to those needed for eventual human application. The relative configuration of the great vessels, in relationship to the heart, is very important to the application and function of these devices. For the uninitiated, these differences in relative size, shape, and configuration may not be familiar.

The most striking difference between quadrupeds and human and nonhuman primates is related to the anterior-posterior alignment of the heart within a narrow, deep thorax, as opposed to a superior-inferior alignment within a flat, wide thorax. This means that the venous return is more or less horizontal and then becomes vertical after entering the right atrium in the normal standing position in quadrupeds. In man, the flow from atrium to ventricle is more horizontal in nature and the inferior vena caval flow is against the gravitational pull. These differences are demonstrated schematically in Figure 1. It does not require much imagination to describe great differences in functional flow dynamics and energetics that can and do result from these differences in gross anatomy. The possible importance of these differences and the role they play in the development of atherogenesis, hypertension, or other disease states await investigation.

Other anatomical variations exist. Cattle and horses typically have a single brachiocephalic trunk that branches off the ascending aorta. This trunk may represent one-third or more of the total cross-sectional

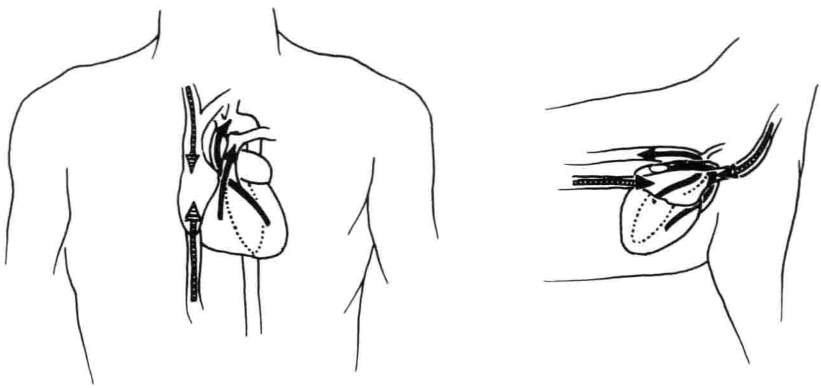

Figure 1. Schematic drawing of the gravitational relationships of the aorta and great veins in upright versus quadruped species.

area of the aorta at that point. Dogs and pigs, typically, have two main branches off the ascending aorta, a brachiocephalic trunk and a left subclavian artery.

Figure 2 is a photograph that compares the ascending aortas from four different species: at bottom left, cow; top left, dog; top right, rabbit; and bottom right, horse. The relative position, size, shape, and configuration of the heart, thorax, and great vessels may be very important in experiments designed to measure input impedance at the semilunar valves, as discussed in Chapters 2 and 3. These data are important for the development of analog and mathematical models of the vascular system. The influence of anatomical differences on these measurements has not been adequately evaluated, but differences in mechanical properties of the vessels, differences in configuration, differences in local flow characteristics, and other anatomical variables could all influence the input impedance seen by the heart.

Histological and Biochemical Properties

Although the basic biochemical components of mammalian myocardial cells have been shown to contain as much as 16 times the normal

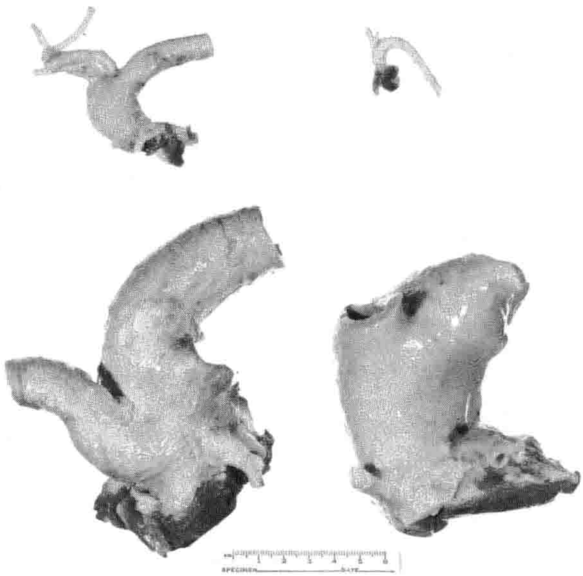

Figure 2. Typical dissected specimens of the ascending aorta from four species. The bottom left is from a cow; top left, from a dog; top right, a rabbit; bottom right, a horse. Each specimen includes the aortic valves, the sinus of Valsalva, the coronary arteries, ascending aorta, first major branches, and a portion of the descending aorta. Note the relative differences in length of the sinus of Valsalva. Also note the variations in angle and conformation of the brachiocephalic trunk as it leaves the aorta.